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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/480,494	06/07/95	ROESKE R	PPI-007

EXAMINER	
BORIN, M	
ART UNIT	PAPER NUMBER
1811	22

18N2/0829

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BOSTON MA 02109-1875

DATE MAILED: 08/29/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

See the attached.

PTO-90C (Rev. 2/95)
*U.S. GPO: 1997-422-198/60031

1- File Copy

Office Action Summary	Application No. 08/480,494	Applicant(s) Roeske R.W.
	Examiner Michael Borin	Group Art Unit 1811

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-47 and 61-81* is/are pending in the application.

Of the above, claim(s) *1-47 and 77-81* is/are withdrawn from consideration.

☒ Claim(s) *73-75* is/are allowed.

☒ Claim(s) *61-68* is/are rejected.

☒ Claim(s) *69, 70, and 72* is/are objected to.

☒ Claims *1-47 and 61-81* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6,16,21*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Pursuant to Preliminary amendment filed 7/2/97 claims 48-60 are canceled, claims 61-81 are added. Claims pending are 1-47,61-81.

2. **Restriction/Election Requirement**

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-47, 48-77 drawn to LHRH peptides and their composition, classified in classes 530, subclass 328, and formulation classified in class 206, subclass 570.

II. Claims 78-79, drawn to methods of inhibiting LHRH activity, classified in class 514, subclass 15.

III. Claim 80 drawn to method of inhibiting a tumor growth, classified in class 514, subclass 15.

IV. Claim 81 drawn to method of inhibiting ovulation, classified in class 514, subclasses 15, 841.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II-IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, methods III-V are alternate

methods of using the compound of Group I. Further, the methods of use III-V can be practiced with a broad variety of LHRH inhibitors beyond the claimed LHRH mimetics.

Groups II-IV are drawn to patentably distinct methods which are not connected in design, operation or effect. The methods are independent if it can be shown that (1) they are not disclosed as capable of use together, (2) they have different modes of operation, (3) they have different functions, or (4) they have different effects. In the instant case, a method of inhibiting LHRH activity, a method of inhibiting growth of a tumor and a method of inhibiting ovulation not disclosed as capable of use together.

If method of Group II is elected, it will be examined together with one of the Groups III or IV.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and the search required for Groups II-IV is not required for Group I, restriction for examination purposes as indicated is proper.

Species Requirement

The claims of Group I are generic to a plurality of disclosed patentably distinct species comprising octapeptides containing dipolar moiety Y (claims 1-16), cationic moiety Z (claims 17-31), receptor-modifying moiety T (claims 32-37), N-acyl hydrophylic moiety M (claims 41-47), small polar moiety L (claims 61-76). Consideration of each group of the claimed compounds requires a separate burdensome search. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

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Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Attorney Catherine J. Kara, on 08/11/97 a provisional election was made with traverse to prosecute the invention of Group I, claims 61-76, drawn to peptides comprising small polar moiety. As per election of species, applicant elected the compound of claim 74. Affirmation of this election must be made by applicant in responding to this Office action. Claims 1-47, 77-81 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Insofar as the elected compound of claim 74 has been found to be neither anticipated nor rendered obvious by the prior art, the Examiner has extended his search to include a reasonable number of additional species within compounds of Group I with small polar moiety, claims 61-76, identified in the Restriction/Election requirement above.

Claim Rejections - 35 USC § 112, second paragraph.

4. Claims 61-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term

"small polar moiety" is a relative term which renders the claim indefinite. The specification does not provide a standard for ascertaining the requisite degree: description of page 7, last paragraph, fails to define a "small steric bulk"for claimed compounds other than the preferred embodiment for which the size is "less than the steric bulk of Trp". Further, the same part of the specification fails to define the limits of another feature, "relatively polar", as the scope of polarity is defined only for some "certain preferred embodiments". Accordingly, it is not possible to determine the metes and bounds of the subject matter that will be protected by the patent grant.

Claim Rejections - 35 USC § 102 and 103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States..

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

6. Claims 61-68,71 are rejected under 35 U.S.C. 102(b) as anticipated by Haviv et al. (US Patent 5,300,492; reference CC), or Haviv ('217), or Xiao et al. (WO 92/08733; ref. CS), or Janecka et al. (Int. J. Peptide and Protein Research, 1994, ref. DO).

Haviv ('492)

Haviv et al. teach peptide LHRH antagonists of formula ABCDEFGHIJ, wherein the radicals which read on the corresponding radicals of the claimed compounds are the following:

A is pyro-Glu, Ac-D-Nal; B is His or 4-Cl-D-Phe; C is Trp, D-Pal, D-Nal, L-Nal, D-Pal(N-O), D-Trp; D is Ser; E is N-Ne-Ala, Tyr, N-Me-Tyr, Lys(iPr), 4-Cl-Phe, His, Ala, Arg, Ile; F is a D-amino acid acyl residue, derived from any natural or synthetic amino acid, such as described in col. 7, lines 5-51;G is Leu or Trp; H is Lys(iPr), Arg, I is Pro, J is Gly-NH2 or D-Ala-NH2. See columns 2-8 under "Disclosure of Invention". Specific compounds, listed in col. 12-25, include LHRH analogs with such residues in position 6 as substituted Ser (columns 14, 24, bottom), substituted Lys (e.g., col. 16), Cit (col. 24, lines 47-55, col. 25, line 43) which read

on the "small polar moiety" of the instant invention. The compounds described by Haviv demonstrate features of LHRH antagonist. See col. 9, lines 10-14 and col.72-74.

Haviv ('217)

Haviv et al teach peptide LHRH antagonists of formula ABCDEFGHIJ, with polar amino acid residues at position, such as substituted D-Serl, D-Ala, D-Lys, etc, which read on the "small polar moiety" of the instant invention. See Summary of invention, col. 1-4, for the complete description of radicals A-J. See col. 3, lines 16-34, specifically describing radical F. See col.9-13 listing preferred compounds. The compounds described by Haviv demonstrate features of LHRH antagonist.

Xiao

Xiao teaches LHRH analogs with various substitutions at position 6, which read on "small polar moiety" of the instant invention, such as Bap, Ea., Pap, Pip, Tep. See specific compounds in Table 1, p. 24 (abbreviations - p. 35). The compounds described by Xiao demonstrate features of LHRH antagonist.

Janecka

Janecka teaches antagonists of peptide structure with acylated lysine and p-aminophenylalanine in position 6, which read on the "small polar moiety" of the instant invention. The title and the abstract disclose the sum and substance of the article.

The compounds specified in Haviv et al. ('492), or Haviv ('217), or Janecka et al. or Xiao inherently possess the properties as set forth in the instant claims. The prior art anticipates the instant invention LHRH antagonist peptide compounds with amino acid at position 6 comprising a small polar moiety. The broad claimed peptides of the instant invention (claims 61-68, 71) are fully met by the referenced peptides. Suggested use limitations do not impart patentability of the product claim where the product is otherwise anticipated by the prior art.

7. Claims 61-68,71 are rejected under 35 U.S.C. 103(a) as obvious over Haviv et al. (US Patent 5,300,492; reference CC), or Haviv ('217), or Xiao et al. (WO 92/08733; ref. CS), or Janecka et al. (Int. J. Peptide and Protein Research, 1994, ref. DO). The references are used as described above. The peptides of the instant art are as close to the prior art as *inter alia*. They are obvious variants and one skilled in the art at the time the invention was made would expect the claimed compounds to have the urged utility.

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: References AA-DR are cited to further show the state of the art, and were provided by applicants.

9. Claims 69, 70, 72-75 are novel and unobvious over the prior art of record or any combination thereof; a diligent search of electronic patent and scientific literature data bases revealed no prior art teaching LHRH

antagonist peptides with D-Asn or D-Gln or D-Thr residues in position corresponding to LHRH position 6. The broad claims of Haviv et al. patents (5,300,492, or 5,110,904 or 5,491,217), encompass LHRH antagonists with the side chain in the position 6 being $(CH_2)_nCOR$, wherein R can be amino, which reads on Gln or Asn. However, no particular subgenuses or compounds with the specified side chain are disclosed, nor there are any teaching suggesting making such species. Coy et al. (J. Med. Chem, 1976, ref. DM) teaches [D-Glu^6]LHRH which exerts features of LHRH agonist, in contrast to [D-Gln] ^{6} derivative of the instant invention which is LHRH antagonist. There would have been no motivation for one of ordinary skill in the art to modify the LHRH antagonists of the prior art in the manner claimed.

10. Claims 73-75 are allowable. Claims 69, 70, 72, 76 are objected to as being dependent upon a rejected base claims, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (703) 305-4506. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Cecilia Tsang can be reached on (703) 308-0254. The fax numbers for this group are (703) 305-3014 and (703) 308-4242.

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Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

August 28, 1997

mlb

CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1800

mlb/ 8/28/97